construction of the term "amplifying" as being limited to non-specific amplification and entered partial summary judgment accordingly.

Vysis contends that the court's decision is based, *inter alia*, on a profound misunderstanding of the prosecution history of the '338 patent and has filed a motion seeking entry of final judgment on the infringement issue so that it can immediately appeal that ruling. While Vysis does so, however, the trial court's ruling on this *infringement* issue should have no effect on resolution of the patentability issues being addressed in these reissue proceedings.

In the first instance, the claim construction urged by Gen-Probe before the trial court is flatly at odds with the claim construction it has advocated in this reissue proceeding. In this reissue proceeding, Gen-Probe filed a Protest against the claims of the '338 patent, asserting invalidity over references that disclosed only specific amplification. For example, Gen-Probe argued that claim 1 was anticipated by Powell et al., *Cell* 50:831-840 (1987), a reference that discloses PCR, perhaps the best known of the specific amplification methods. See Protest, pp. 23-25.

Second, the court's decision is currently a "partial summary judgment" that is not yet a final, appealable court decision. Rule 54(b), Fed. R. Civ. P. The Patent Owner is presently seeking to convert that order into a final judgment so that it can promptly appeal, but that relief has not yet been granted. The Patent Owner will apprise the PTO of developments in this regard as they occur.

Third, the court's decision is not a decision on the validity of the '338 patent. Indeed, the court expressly recognized that "a motion for invalidity pursuant to 35 U.S.C. § 112 is not before the Court." Order, p. 7, line 19. The court's decision is directed to issues of *infringement* and does not control resolution of the issues of *patentability* that are currently before the PTO.

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Fourth, and perhaps most importantly, the court's decision is not logically compelling because it is based on a manifest misunderstanding of the prosecution history of the original '338 patent that should be clear to the PTO even in advance of appellate review of that decision. While it is true that the specification does not use the term "PCR," neither does it limit the invention to non-specific amplification. The absence of any detailed discussion of amplification methods is not remarkable because the inventors of the '338 patent had not invented amplification. Both specific and non-specific amplification methods were well known in the art, and the PTO so held repeatedly and without contradiction from the Patent Owner in the original prosecution. Instead, the invention related to the combination of target capture with amplification. That combination permits the use of non-specific primers for the amplification step, but does not require the use of non-specific primers. And while the specification highlights the benefits of the combination of target capture and non-specific amplification, it does not limit the claimed combination to non-specific amplification.

The prosecution history of the '338 patent bears this out. Each of the five Examiners who evaluated the application and its related counterparts recognized that amplification encompassed specific amplification as in PCR. Indeed, the substantive examination of the '338 patent began with a rejection for obviousness under 35 U.S.C. § 103 "over Mullis [the PCR patent] when taken with any of Moss et al., Stabinsky or Engelhardt et al. and taken further in view of Ranki et al. or Josephson et al. or Schroder if necessary." *See* USSN 07/944,505, Office Action of Nov. 5, 1992, at pp. 3-4. The Examiner explained that:

> The primary reference teaches DNA amplification and point[s] out the great value of this method for improved sensitivity as well as improved ability to isolate specific nucleotide sequences. The primary references do not specifically teach nucleic acid affinity chromatography prior to the amplification reaction. The secondary references all teach the well known method of affinity

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> chromatography. * * * It would be obvious for one of ordinary skill in the art to combine the teachings of the primary references which show improved sensitivity and improved ability to purify a sequence with the secondary references which teach a method providing improved ability to purify a sequence and improved sensitivity since the methods are all directed to the same result and one of ordinary skill would expect an improvement in results.

Id. That this was *not* a rejection alleging obviousness of *non-specific* amplification is clear from the separate treatment of dependent claims requiring non-specific amplification in that same Office Action, based on a different technique which the PTO also characterized as "well known." *Id.* at 4.

Of course, the inventors never distinguished the claims as not encompassing PCR, but rather focused on the lack of any suggestion for the combination of PCR with target capture. *See* USSN 08/283,080, Preliminary Amendment and Response to Restriction Requirement of Dec. 5, 1995, pp. 11-12 and 15-20. The Examiners' belief that the claims expressly covered PCR was so fundamental to the examination that the Examiner who allowed the '338 Patent concluded in the Statement of Reasons for Allowance that:

> The claims are drawn to methods of PCR amplification wherein the target is first separated from the sample by using a support that binds to the target polynucleotide and then amplified.
>
> * * *
>
> [T]he art at the time of filing did not recognize that the efficiency of PCR amplification would decrease due to the presence of contaminants in a sample and therefore provided no motivation to purify a target sample from a heterogeneous sample of nucleic acids prior to amplification. Having not recognized the problem, applicant's solution therefore, while utilizing routine methodology to modify PCR amplification, would not have been obvious at the time the invention was made.

USSN 08/238,080, Notice of Allowability of Oct. 13, 1997.

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Gen-Probe completely ignored this prosecution history in its opening brief in support of its motion, but its reply brief urged that the PTO had not really rejected the claims as encompassing PCR, as follows:

> Vysis' initial applications were not rejected by the PTO because Vysis' claims encompassed PCR, but because those claims were an "obvious" attempt to achieve the same result as PCR in a different manner.

Gen-Probe's Reply Memorandum, p. 14. The trial court accepted this contention, holding:

> Gen-Probe asserts that the rejection by the PTO of the patent application based on the Mullis (PCR) patent does not support the claim that the patent covered PCR amplification methods. Vysis acknowledged in oral argument that [it] did not have a license to the Mullis patents or PCR method. Gen-Probe argues that the patent application was rejected as obvious in light of the PCR patents because specific capture methods plus non-specific amplification were an attempt to achieve the same results as PCR. . . .
>
> * * * *
>
> The Court concludes that the references to the Mullis patents and PCR in the prosecution history do not help clarify the proper construction of the term "amplifying" as used in the '338 patent. At most, the prosecution history indicates that the idea of amplification by first using specific target capture techniques is close enough to the goals of PCR to be "obvious" to the PTO in light of the Mullis patents. [Footnote omitted.]

Slip op. at 8-9. The Statement of Reasons for Allowance and the separate treatment of claims directed to non-specific amplification demonstrate the error in Gen-Probe's contention and the court's holding. It could not be clearer that the '338 patent claims were repeatedly rejected precisely because they encompassed specific amplification techniques such as PCR. The court's holding is manifestly based, at least in part, on a fundamental misunderstanding of the prosecution history.

In order to avoid any ambiguity as to the scope of the amplification techniques encompassed by the claims, the Patent Owner wishes to add to its previously submitted intermediate scope claims dependent claims that recite "random primers" and "specially tailored primers." These amendments are made in the accompanying Supplemental Preliminary Amendment and are fully supported by the original specification.

If there are any fees due with the filing of this Notice not already accounted for, please charge the fees to our Deposit Account No. 06-0916

Respectfully submitted,

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Dated: July 16, 2001

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